8. Evaluación de riesgos

Los niveles de tolerancia válidos actualmente para las ficotoxinas, se basan principalmente en datos de incidentes de intoxicación. Sin embargo, son pocas veces precisos y completos limitándose a toxicidad aguda. En algunos casos, el nivel de tolerancia se adapta también a las limitaciones del método de detección. Para el análisis de riesgos, debieran normalizarse los niveles de ingesta de mariscos en los seres humanos.

8.1 Evaluación de riesgos para la intoxicación paralítica por mariscos (PSP)

La evaluación toxicológica de riesgos para las toxinas PSP puede basarse actualmente sólo en datos de toxicidad aguda. No hay disponibles datos subcrónicos y crónicos ni para animales ni para seres humanos. Las menores dosis que ocasionan síntomas leves de PSP en los seres humanos varían entre los 120 y los 304 µg/persona, en tanto que las más bajas asociadas con intoxicaciones/muertes severas están entre los 456 y los 576 µg STX/persona. Comúnmente se aplica, para proteger a las personas más susceptibles (niños, ancianos, enfermos), basado en datos de seres humanos, un factor de incertidumbre de 10 para calcular los valores de la ingesta diaria total para los contaminantes. Sin embargo, en los cálculos para la PSP debe tenerse en cuenta a qué niveles los efectos deben considerarse "adversos" y cuál es el nivel real para los NOAEL y LOAEL. Por otra parte, como los datos de PSP representan a muchos individuos con grandes diferencias en sus susceptibilidades, puede no ser necesario un factor de 10 (Aune, 2001). La mayoría de los países utilizan un factor de tolerancia de 80 µg STX eq/100 g de carne de mejillones. Si se estima el consumo de mariscos entre 100 y 300 g/comida, existe un margen de seguridad de alrededor de < 1 a 3,8 para los síntomas leves y, más importante, un margen de seguridad de sólo 1,9 a 7,2 para las intoxicaciones graves y la muerte. Estos son, o márgenes muy pequeños o bien no hay margen alguno.

No obstante, no resulta ni práctico ni realista fijar un nivel de tolerancia muy bajo al ser el método para determinar las toxinas PSP más extensamente empleado en la actualidad el bioensayo en ratón con un límite de detección de aproximadamente 40 µg PSP (STX eq)/100 g marisco. Una vez que se disponga de análisis químicos más sensibles (y confiables), debieran examinarse nuevamente los valores de toxicidad del STX y sus derivados para exposiciones agudas y subcrónicas.

8.2 Evaluación de riesgos para la intoxicación diarreica por mariscos (DSP)

Las diferentes toxinas en el complejo DSP pueden dividirse en tres grupos, el ácido ocadaico y las DTXs, las PTXs y las YTXs, estructuralmente vinculadas.

Un Grupo de Trabajo de la UE de Toxicología de las DSP y de las AZP ha recomendado niveles de tolerancia para estos tres grupos de toxinas DSP (EU/SANCO, 2001).

OA y DTXs

En las experiencias con animales, los efectos genotóxicos y cancerígenos de las OA y de las DTXs se aprecian a dosis relativamente altas y con periodos de exposición prolongados, comparativamente con los niveles causantes de diarreas en seres humanos poco después del consumo de mariscos contaminados. Es, entonces, poco probable que exista en los consumidores de mariscos un riesgo sustancial de cáncer debido a estas toxinas. En consecuencia, la evaluación de riesgos en los seres humanos está basado en un N(L)OAEL sobre datos de animales y seres humanos con un factor de incertidumbre. De disponerse, son preferibles, los datos en seres humanos.

Puede concluirse, tomando en cuenta todos los datos de exposición para seres humanos, que los niveles más bajos que resultan en efectos diarreicos van de 32 a 55 µg OA y/o DTX1. Estos valores surgen de informaciones japonesas y noruegas. Los efectos parecen limitarse a diarreas, vómitos, dolores de cabeza y malestar general. A estos niveles no se han apreciado efectos serios o irreversibles sobre la salud (EU/SANCO, 2001). Los reglamentos europeos vigentes permiten valores máximos conjuntos de OA, DTXs y PTXs de 160 µg OA eq/kg de tejido edible. Estimando que el consumo de mariscos está entre 100 y 300 g/comida, existe un margen de seguridad de cerca de < 1 a 3,4 para los efectos diarreicos. Estos márgenes son o muy pequeños o bien no existe margen alguno. EU/SANCO (2001) sostiene que si el nivel de OA y de DTXs en los mariscos no supera los 16 µg/100 g de carne de marisco, no existen riesgos apreciables para la salud con consumos de 100 g de carne de mejillones diarios.

PTXs

No se dispone de datos para seres humanos de PTXs. El nivel de seguridad para los seres humanos se basa, entonces, en datos toxicológicos de animales. Sólo se dispone de datos de toxicidad en animales para las toxinas PTX2, del grupo de las PTX. No se sabe de efectos de inducción o promoción de tumores. Se ha informado un valor de 0,25 mg/kg pc para el LOAEL de la PTX2 administrada oralmente a los ratones, basado en los efectos diarreicos y hepáticos. El NOAEL debiera estimarse aplicando un factor de 10 al LOAEL. Para extrapolar los datos de animales a los riesgos en seres humanos se aplica un factor de 100. Resulta así, que aplicando un factor de incertidumbre de 1 000, puede calcularse un nivel de seguridad de 0,25 µg/kg pc para los seres humanos ~ 15 µg para un adulto con 60 kg de peso. EU/SANCO (2001) ha recomendado un nivel de tolerancia de 15 µg/100 g de carne de marisco. No obstante, si el consumo de mariscos se estima entre 100 y 300 g por comida, el nivel de tolerancia debe estar entre 5 y 15 µg/100 g de tejido edible de mariscos.

Se dispone de datos de exposición para los seres humanos para el ácido seco PTX2 (PTX2-SA), resultantes de un caso de intoxicación por el marisco pipi (56 casos de hospitalización) en Nueva Gales del Sur (Australia) en diciembre de 1997 (ANZFA, 2001). Según Quilliam *et al*. (2000), la PTX2-SA puede haber contribuido a los síntomas gastrointestinales, los vómitos o la diarrea en los seres humanos (Aune, 2001). Burgess y Shaw (2001) informaron que los pacientes habían consumido aproximadamente 500 g de pipis conteniendo 300 µg de PTX-2SA/kg (~150 µg PTX-2SA/persona ~2.5 µg/kg pc para una persona con un peso de 60 kg). Aplicando un factor de incertidumbre de 100 (10 para diferencias entre las especies y de 10 para extrapolaciones de LOAEL a NOAEL) (~1.5 µg/persona con un peso de 60 kg) puede calcularse un nivel seguro para los seres humanos de 0,025 µg/kg pc para la PTX-2SA. Esto implica que para la PTX2-SA, el nivel de tolerancia debe estar entre 0,5 y 1,5 µg/100 g de tejido edible con consumos entre 100 y 300 g por comida.

YTXs

No hay información disponible en seres humanos para las YTXs. El nivel de seguridad está, por tanto, basado en datos para animales. Se estimó el NOAEL en los ratones en 1,0 mg/kg pc mediante administración oral aguda basada en los efectos cardíacos. Se ha calculado un nivel de seguridad para los seres humanos de 10 µg/kg pc para efectos tóxicos agudos YTX con un factor de incertidumbre de 100. Para un adulto con un peso de 60 kg, esto representaría un nivel de seguridad de 600 µg de YTX. Dada la ausencia de datos para administraciones repetidas, y el factor de incertidumbre elevado recomendado por la OMS para una sustancia que lesiona los músculos cardiacos, el nivel indicado de seguridad calculado para los seres humanos podría reducirse en un factor de 6 a 100 µg (EU/SANCO, 2001). EU/SANCO (2001) recomendó un nivel de tolerancia de of 100 µg de YTXs/100 g de carne de marisco. Sin embargo, si se estima el consumo de mariscos entre 100 y 300 g por comida, el nivel de tolerancia debe situarse entre 33 y 100 µg/100 g de tejido edible de mariscos.

8.3 Evaluación de riesgos para la intoxicación amnésica por mariscos (ASP)

El valor guía generalmente aplicado de 20 mg DA/kg de mejillones, resulta de un incidente de ASP en el Canadá (Isla Príncipe Eduardo) y ha sido adoptado por varios países. El valor guía de 20 mg DA/kg resulta de una ingesta de 0,03 a 0,1 mg DA/kg pc por persona con un peso corporal de 60 kg y para un consumo de mejillones de entre 100 y 300 g/comida. Los datos epidemiológicos empleados para deducir el valor guía, revelaron efectos gastrointestinales moderados en los seres humanos para 1 mg DA/kg pc. Con posterioridad el valor guía fue evaluado en estudios agudos con animales. Sin embargo, al comparar las dosis necesarias para causar toxicidades evidentes en especies animales, ratones y ratas parecían ser relativamente insensibles comparados con las de monos y con las dosis orales que requerían más toxinas (más de 10 veces en los roedores) para alcanzar los mismos efectos que con una dosificación i.p. Las ratas mostraron efectos evidentes de intoxicación con DA con dosis orales únicas de unos 80 mg/kg pc, en tanto que los monos tenían vómitos, arcadas y bostezos ya a valores de 1 mg/kg de pc. Una única dosis oral de 0,75 mg de DA/kg de pc en monos no produjo efectos evidentes. Esta sensibilidad, aparentemente disminuida, de los roedores puede resultar de su ineptitud para vomitar y/o del hecho de que la vida media del plasma del DA en la rata es unas 6 veces menor que la del mono. Comparando el valor guía de 20 mg DA/kg de tejido de mejillones (~ 0.1 mg/kg pc para seres humanos y suponiendo un consumo de 300 g de mejillones por comida) con la dosis sin-efecto (0,75 mg/kg pc) en estudios orales agudos con monos, entre estos valores aparece un factor menor de 10. Se desconocen los efectos de exposiciones prolongadas a niveles bajos de DA. Sin embargo, los estudios de corto plazo con animales con exposiciones repetidas no apuntan a una eliminación alterada del DA del suero o a respuestas neurotóxicas superiores a las resultantes de exposiciones simples.

Para las 10 personas involucradas en el incidente canadiense (personas mayores con edades entre los 60 y los 84 años) pudieron determinarse datos dosis-respuesta razonablemente buenos. De acuerdo con estos datos el NOAEL era de 0,2-0,3 mg DA/kg pc, en tanto que el LOAEL de 0,9-2,0 mg DA/kg pc para intoxicaciones serias registradas con valores de 1,9 a 4,2 mg DA/kg pc. Resulta interesante que las estimaciones de ingesta mostraron consumos sorprendentemente elevados de mejillones azules, 120 a 400 g de carne de mejillones por persona y por comida (Aune, 2001). Esto implica que hay un factor dos ente el NOAEL y el límite reglamentario de 20 mg DA/kg de carne de mejillones que equivale a 0,1 mg/kg pc para una persona de 60 kg de peso que consume 300 g de carne de mejillones por comida. Entre el LOAEL y el límite reglamentario hay un margen de 9 a 20 y entre el nivel de efectos serios y el límite reglamentario el margen es de 19 a 42.

8.4 Evaluación de riesgos para la intoxicación neurológica por mariscos (NSP)

No es posible el análisis de riesgos por falta de suficientes datos toxicológicos y por las dificultades analíticas relacionadas con la determinación de la exposición a la brevetoxina. La gestión de riesgos que se realiza actualmente (en los estados costeros del Golfo de México) se basa en el cierre de las bases de mariscos a valores de 5000 *G. breve* células/litro volviéndose a abrir cuando la determinación de la Tx en los mariscos es menor a 80 µg/100 g.

8.5 Evaluación de riesgos para la intoxicación azaspiracida por mariscos (AZP)

EU/SANCO (2001), basado en incidentes de intoxicaciones en Irlanda, afirma que los niveles de AZAs calculados y causantes de intoxicaciones en seres humanos están entre 6,7 y 24,9 µg. Estos valores incluían una disminución en el contenido de AZA resultante del calentamiento de los mejillones. Los nuevos datos de estabilidad térmica indican que estaba justificada esta reducción del contenido de toxinas debida al calentamiento. En consecuencia, el rango nuevamente calculado para el nivel mínimo con efecto adverso observable (LOAEL) parecía estar entre 23 y 86 µg por persona suponiendo un consumo máximo de 100 g de mariscos por comida. EU/SANCO (2001) aplicaron un factor de seguridad de tres para convertir el LOAEL en un NOAEL. Basándose en un nivel de ingesta con un máximo de 100 g de carne de marisco/comida y con el LOAEL más bajo dividido por tres,

EU/SANCO (2001) afirman que un nivel de tolerancia de 8 µg AZAs/100 g de marisco debiera resultar en un riesgo no apreciable para la salud humana. Se ha sugerido un nivel de 16 µg/100 g para permitir la detección por el bioensayo en ratón. Sin embargo, con consumos de mariscos de 300 g por comida, un individuo ya ingeriría una cantidad de AZAs equivalente al LOAEL para seres humanos.

Ofuji *et al*. (1999b) informaron en incidentes de intoxicación un nivel de 1,4 µg/g para el AZAs total en carne cruda de mejillones. Esto equivale a una ingesta de 140 a 420 µg AZAs/persona, con consumos de 100 a 300 g por comida. Para calcular el NOAEL se aplica comúnmente un factor de 10 por representar estos valores un nivel de efecto (LOAEL). Esto significa que el NOAEL es de 14 a 42 µg por persona suponiendo un consumo de 100 a 300 g de carne de mariscos/comida. Como resultado el nivel de tolerancia para la carne de mariscos debe ser de 14 µg/100 g. Debe señalarse que no se aplicó un factor de 10 al NOAEL para tener en cuenta las diferencias entre especies (variación en la población humana).

8.6 Evaluación de riesgos para la intoxicación por ciguatera en pescado (CFP)

Los datos disponibles sobre ciguatera para animales no son adecuados para un análisis de riesgos. En consecuencia, debieran emplearse datos de seres humanos resultantes de incidentes de intoxicación.

Son de esperar ya síntomas ligeros de CFP en algunos individuos luego de ingerir pescados con la principal ciguatoxina del Pacífico (la P-CTX-1) en un nivel de 0,1 µg/kg. La principal ciguatoxina del Caribe (C-CTX-1) es menos polar y 10 veces menos tóxica que la P-CTX-1. Suponiendo consumos de pescado de 500 g por comida y un peso corporal del ser humano de 50 kg, esto se corresponde con 0,001 µg/kg pc (=LOAEL). Estos valores resultan de un servicio importante de comidas con el pescado menos tóxico causante de efectos en algunos seres humanos. Es de esperar que un nivel de 0,01 µg/kg pc resulte tóxico para la mayoría de las personas por ser diez veces superior al nivel responsable de síntomas ligeros en algunos individuos. Puede calcularse un nivel “seguro” de 0,01 µg/kg de carne de pescado, empleando un factor de incertidumbre de 10 (por las diferencias entre especies) al menor nivel responsables de síntomas suaves en los seres humanos (=LOAEL), (Lehane, 2000; Lehane y Lewis, 2000). Debe señalarse que no se utilizó el factor de incertidumbre habitual de 10 sobre el LOAEL para calcular el NOAEL.

8.7 Comentarios finales

La evaluación de riesgos para las ficotoxinas no se ha realizado, hasta el momento, de manera simple. El proceso se ha complicado al mezclarse la evaluación de riesgo y la gestión de riesgos. Hay, en general, carencias de datos toxicológicos particularmente para las exposiciones repetidas. Con sus propias limitaciones, se disponía de datos epidemiológicos de incidentes de intoxicaciones, lo que permitió evaluaciones de riesgo provisorias para algunas ficotoxinas, las que no siempre fueron lógicas y consistentes. Para algunas ficotoxinas, la evaluación de riesgos no se ha podido realizar por falta de un mínimo de datos.

De disponerse de datos científicos adecuados (toxicológicos, epidemiológicos y de presencia), podría hacerse una evaluación de riesgos empleando factores de seguridad y de incertidumbre aceptados generalmente. Con conjuntos adecuados de datos para animales, puede deducirse el nivel sin efecto adverso observable (NOAEL). Para los seres humanos puede calcularse un nivel seguro empleando para el NOAEL un factor de incertidumbre de 100 (10 para diferencias entre especies y 10 para diferencias intra especies). De disponerse de un conjunto adecuado de datos para seres humanos un nivel seguro resulta de aplicar un factor de incertidumbre de 10 al NOAEL (para tener en cuenta las diferencias intra especies), resultante de esos datos sobre humanos.

9. Conclusiones y recomendaciones

9.1 Conclusiones

El consumo de diversos mariscos y pescados ocasiona mundialmente un número creciente de intoxicaciones en los seres humanos. El diagnóstico se basa principalmente en el reconocimiento de señales y síntomas específicos y en la identificación de las toxinas marinas presentes en los frutos del mar. Debido a los métodos analíticos inadecuados, habitualmente no se dispone ni de indicadores de los efectos ni de la exposición, para las a veces complejas mezclas de toxinas de algas. Por lo general sus efectos se observan como intoxicaciones agudas. Apenas se conocen los efectos resultantes sobre la salud de exposiciones episódicas y de la exposición crónica a niveles bajos de toxinas de algas. Estos últimos efectos pueden pasar sin ser informados por el o los individuos afectados o ser objeto de diagnósticos médicos erróneos.

Para la gestión de riesgos es esencial el seguimiento de la toxicidad de los frutos del mar. No obstante, existen diversas limitaciones, como las variaciones en el contenido de toxinas entre mariscos tomados individualmente, los diferentes métodos de detección y aun de extracción para las diferentes toxinas que requieren decidir cuales son las toxinas a ensayar y la frecuencia del muestreo que asegure que la toxicidad no alcance niveles peligrosos entre los tiempos y los lugares de muestreo, tanto en el tiempo como en el espacio. Pueden, además, incrementar los problemas sanitarios en los seres humanos y las responsabilidades de gestión, las crecientes cosechas de mariscos no tradicionales (como caracoles de la luna**,** busicones, percebes, etc.).

Un seguimiento del plancton tóxico permitiría posiblemente superar algunos de estos problemas. Sin embargo, las poblaciones de plancton son efímeras y espaciadas y resulta difícil establecer una correlación cuantitativa entre la cantidad de plancton tóxico y los niveles de toxinas en los mariscos y la cantidad de toxina por célula, muy variable. Los datos de presencia de especies de toxinas de algas pueden indicar cuales son las toxinas esperables durante los periodos de floración de las algas y cuales productos de mariscos debieran considerarse para el seguimiento analítico. Un problema es que algunas especies de algas, desconocidas en una zona determinada, pueden aparecer de manera repentina y causar problemas rápidamente. Las observaciones sobre el plancton se emplean para dirigir los ensayos de toxicidad, pero no para adoptar decisiones reglamentarias sin otro tratamiento. Más aun, la mayor parte de los programas de seguimiento y reglamentarios son con frecuencia inadecuados para enfrentar las crecientes amenazas de las nuevas floraciones de algas perjudiciales. Como resultado, cuando ocurren nuevos brotes, la respuesta es frecuentemente lenta y no coordinada. Las floraciones de algas son impredecibles y la información sobre su inicio escasa.

Las floraciones tóxicas se detectan fundamentalmente por confirmación visual (decoloración de las aguas y mortandad de peces), enfermedades en personas que han consumido mariscos y/o irritación respiratoria, aunque la toxicidad real sea solo verificada mediante largos bioensayos en ratón y análisis químicos de muestras de mariscos. Esta estrategia “posterior a los hechos” resulta de las grandes dificultades para predecir la presencia y magnitud de la floración. Para evitar la contaminación de seres humanos, son en general suficientes programas de seguimiento basados en la enumeración e identificación microbiológica de las especies perjudiciales en las muestras de aguas. Las técnicas de seguimiento microscópico, sin embargo, requieren de una alta habilidad taxonómica, son largas y, dependiendo de la persona que las realice, muy variables.

Uno de los problemas más serios es la falta de información sobre la biología de las algas perjudiciales es., Se sabe muy poco, por ejemplo, de la abundancia, distribución, dinámica poblacional y fisiología de las especies más perjudiciales, tanto en aguas locales como de otras zonas. Es esencial el seguimiento rutinario y de largo plazo del fitoplancton y del medio ambiente, para obtener los datos necesarios que permitan determinar, al menos, la ecología más elemental de las especies perjudiciales. Además, por ser compleja la dinámica de la floración, los factores determinantes en una zona geográfica, en particular pueden no afectar la misma especie en otra zona, aunque próxima. En

consecuencia, son deseables sistemas de evaluación alternativos para predecir la ocurrencia de floraciones.

Son diversos los factores que juegan para fijar criterios reglamentarios y límites para las toxinas marinas; como la disponibilidad de datos de encuestas, de datos toxicológicos, de la distribución de las toxinas en los lotes muestreados y de la estabilidad de las muestras, de métodos analíticos y de reglamentaciones ya vigentes en diferentes países. Respecto a la toxicidad, hasta ahora sólo se dispone para la mayoría de las toxinas marinas de datos de toxicidad oral aguda tanto para animales de laboratorio como para seres humanos. Sin embargo, puede ser frecuente la exposición repetida a niveles de dosis subletales.

En lo que hace a los métodos de detección, existe una necesidad mundialmente generalizada de que sean rápidos, confiables y sensibles para la determinación de las toxinas marinas en mariscos y pescados. El bioensayo en ratón disponible actualmente no resulta lo suficientemente sensible, lleva tiempo, es susceptible a las interferencias y no ético respecto al bienestar de los animales. Quilliam (1998b) aboga por el empleo de la CL-EM como método de detección universal para todas las toxinas marinas. Esta técnica ofrece un bajo límite de detección, una alta sensibilidad y la capacidad de enfrentar la diversidad estructural y la naturaleza lábil de las toxinas. Además, hace posible la separación de mezclas complejas, su determinación cuantitativa exacta y precisa, la automatización y un elevado número de análisis, con resultados aceptables legalmente para confirmar toxinas y obtener información estructural de nuevas toxinas.

Otro nuevo desarrollo prometedor son los biosensores con los que pueden determinarse simultáneamente multiplicidad de toxinas.

Puede acelerarse el desarrollo y el empleo de nuevos métodos analíticos, idóneos y eficientes, suministrando información de manera rápida y adecuada, por ejemplo, mediante una base de datos accesible por Internet. La base de datos debe incluir los nombres químicos, las propiedades físicas/químicas, las clasificaciones, el o los efectos tóxicos, las fuentes, el hábitat, los límites reglamentarios y referencias bibliográficas.

9.1.1 Conclusiones relativas a la intoxicación paralítica por mariscos (PSP)

Los niveles de tolerancia fijados para las toxinas PSP son hasta ahora decisiones prácticas basadas en casos de intoxicación y aunque haya muchos casos informados debidamente de intoxicaciones de seres humanos atribuibles a las toxinas de mariscos, resulta difícil obtener datos de toxicidad humana *confiables*. Por ejemplo, las variaciones observadas en la toxicidad humana de las toxinas PSP pueden no sólo deberse a variaciones en la sensibilidad entre personas sino también a la composición de las toxinas individuales en las muestras. Los perfiles de las toxinas pueden variar según la especie de marisco consumido y la zona de cosecha. Además, las dosis toxicas se estiman con frecuencia sobre restos de alimentos marinos. Estos no son necesariamente representativos de los alimentos ingeridos pues las toxinas PSP pueden estar distribuidas irregularmente en los lotes y dentro de los propios mariscos individuales, además de no ser todas las toxinas PSP estables.

Los diversos métodos analíticos con los que es posible medir los compuestos de PSP tienen todos limitaciones y a menudo no son fácilmente realizables debido a la falta de materiales de referencia, pese a los recientes avances en este campo. En el año 2003, había disponibles comercialmente estándares certificados de las toxinas STX, neoSTX, dc-STX, GNTX 1-4, GNTX 2/3 y GNTX 5. Sin embargo, resultan costosos y disponibles básicamente de una única fuente. Aun así, mejora significativamente con ellos la calidad de los datos obtenibles con los métodos de CL. Los esfuerzos del Programa de Normas, Medidas y Ensayos de la Comisión Europea, han resultado en materiales de referencia para mariscos con fracciones de masa certificadas para algunas de las toxinas PSP toxicológicamente más significativas. A pesar de estos desarrollos positivos, la situación analítica permanece difícil y la falta de compuestos PSP puros en cantidades suficientes para estudios repetidos

de dosis de toxicidad resulta un factor limitante para el desarrollo de una evaluación de riesgos confiable.

9.1.2 Conclusiones relativas a la intoxicación diarreica por mariscos (DSP)

La variedad de actividades biológicas de las toxinas DSP puede causar algunos problemas. Aunque las PTXs y YTXs resultan agudamente tóxicas en ratones luego de inyecciones i.p., se desconoce su toxicidad oral en seres humanos. En consecuencia, debe disponerse de más datos toxicológicos de las PTXs y de las YTXs. Además, la OA y la DTX poseen actividad promotora de tumores, en tanto que la OA muestra también actividad genotóxica e inmunotóxica. Estos efectos plantean preguntas sobre los riesgos para la salud humana a exposiciones subcrónicas a niveles bajos de estos compuestos. Un problema acuciante es la falta de cantidades suficientes de toxinas DSP que permitan realizar estudios de toxicidad subcrónica en animales.

Aunque se aplican mundialmente, los bioensayos para la toxicidad DSP, hay una gran diferencia en el comportamiento de, por ejemplo, el bioensayo en ratón (el punto final de la toxicidad es la muerte del animal; sin consenso sobre el tiempo de observación adecuado) en los diferentes países, lo que resulta en diferencias de especificidad y detectabilidad. Un problema importante es que los bioensayos en ratón detectan todos los componentes de la DSP y quizás también otras toxinas. Sin embargo, no es posible distinguir entre las diferentes toxinas aun cuando se han fijado límites legales específicos para los grupos de toxinas (por ejemplo en la UE). Por otra parte, los bioensayos en ratas sólo detectan la OA y las DTXs por ser los puntos finales de este análisis heces blandas, diarreas y rechazo de los alimentos que se sabe son sólo causados por las OA y las DTXs (y las AZAs).

Los métodos químicos (CL) resultan útiles para la identificación y cuantificación de toxinas diarreicas seleccionadas (en general OA o DTXs). Recientemente se desarrolló un método de CL para la detección de YTXs, pero hasta el momento no se dispone de ninguno para las PTXs salvo la CL-EM, que no es aun satisfactorio. Los métodos químicos se emplean como una herramienta reglamentaria para confirmar los resultados obtenidos de un bioensayo.
Ninguna de las muchas aproximaciones empleadas para la determinación de la DSP en mariscos ha sido formalmente evaluada mediante estudios colaborativos de la ISO/IUPAC/AOAC por lo que las características de funcionamiento no son conocidas completamente. El desarrollo posterior, la evaluación y la comparación de las diversas técnicas resultaría significativamente más simple de poderse desarrollar y poner a disposición de la comunidad científica estándares y materiales de referencia confiables (como muestras de mejillones liofilizadas y con contenido certificado de las diferentes toxinas DSP).

9.1.3 Conclusiones relativas a la intoxicación amnésica por mariscos (ASP)

Los problemas derivados de las toxinas amnésicas de los mariscos son comparativamente de menor magnitud que los resultantes de los paralíticos y diarreicos. El único brote confirmado e informado a nivel mundial de ASP, resultante en enfermedades graves, tuvo lugar en 1987 en la Isla Príncipe Eduardo, Canadá. Con posterioridad al primer brote en el Canadá, solamente se observaron enfermedades en seres humanos (benignas y cortas) en un brote causado por el consumo de navajuelas contaminadas (de la costa oeste de los Estados Unidos). Las autoridades sanitarias, sin embargo, no pudieron confirmar que la DA fuese responsable por las enfermedades. En dos brotes, se informó de la muerte de cormoranes y/o de pelícanos marrones por consumo de anchoas y caballas contaminadas, lo que indica que los peces herbívoros pueden ser vectores de la DA. La DA también fue recientemente detectada en mariscos de algunos países europeos (1999 a 2002).

Los métodos analíticos para la DA son bastante simples y menos complejos que los requeridos para analizar las toxinas paralíticas y diarreicas en mariscos. Se ha validado exitosamente un método químico para determinar el DA en los mejillones (CL con detector UV) en estudios colaborativos

formales, en tanto que otro método (mejorado) está siendo actualmente objeto de un estudio colaborativo. Se obtienen fácilmente los materiales de referencia certificados y para calibraciones.

9.1.4 Conclusiones relativas a la intoxicación neurológica por mariscos (NSP)

Son posibles diferentes rutas de exposición de los seres humanos a las brevetoxinas; la ruta oral mediante el consumo de mariscos contaminados, la ruta inhalatoria mediante la exposición a brevetoxinas bajo forma de aerosol y la ruta dérmica mediante contacto directo con agua de mar contaminada. Los efectos de las diferentes rutas de exposición en seres humanos son de difícil evaluación al ser limitados los datos de toxicidad de las brevetoxinas. Se dispone de algunos estudios agudos en ratones y de datos de casos de intoxicación en seres humanos y mamíferos marinos; faltan, sin embargo, estudios dérmicos agudos y de inhalación, así como estudios orales, dérmicos y de inhalación con animales de laboratorio sometidos a exposiciones repetidas. No es posible, en consecuencia, realizar la evaluación de peligros.

Para realizar estudios de toxicidad serían necesarias toxinas puras y sus metabolitos. Además, para desarrollar y mejorar aun más la metodología analítica y para permitir el aseguramiento analítico de los laboratorios de control, serían necesarios materiales de referencia analíticos. Actualmente los diferentes obstáculos para una evaluación confiable de la presencia y de la exposición de las brevetoxinas dificultan proseguir con la evaluación de riesgos y, en consecuencia, fijar reglamentos significativos.

A pesar de estos problemas, en unos pocos países hay vigentes reglamentos para las toxinas NSP en mariscos, basadas en bioensayos en ratones, particularmente en los Estados Unidos, Italia y Nueva Zelanda. El nivel de acción es de 20 MU/100 g carne de mariscos (~80 μg PbTx-2/100 g carne de marisco).

9.1.5 Conclusiones relativas a la intoxicación por azaspiracida en mariscos (AZP)

Un motivo de preocupación son los tumores de pulmón en ratones luego de dosis repetidas de 20 μg AZA/kg pc y superiores. Esto debiera confirmarse con experiencias involucrando una cantidad mayor de ratones y periodos de exposición más prolongados (Ito *et al*., 2002).

El actual nivel de tolerancia debe revisarse a medida que se disponga de nuevos datos. Sin embargo, en todos los estudios, un serio obstáculo es carecer de toxinas puras. A su vez, la producción de toxinas puras requiere disponer de cantidades importantes de mejillones tóxicos. Debiera explorarse el desarrollo de métodos de detección rápidos del tipo de la CL-con detector de fluorescencia (DFL), ELISA y ensayos funcionales.

9.1.6 Conclusiones relativas a la intoxicación ciguatera en pescado (CFP)

La intoxicación por ciguatera tiene lugar principalmente en las regiones tropicales del planeta, siendo esporádica en Europa, particularmente en los países de Europa del norte. Para aquellos países fuera de una zona en que la CFP es endémica, resulta adecuado un control analítico regular de las ciguatoxinas en los pescados importados predatorios de gran tamaño.

Hay pocos reglamentos específicos para las ciguatoxinas. Un resultado positivo en un pescado determina su retiro de la venta. A veces, sin analizar la toxina, se imponen restricciones a la venta de pescados de determinadas especies o tamaños provenientes de una zona en particular. Cuanto mayor sea el pescado, seguramente más edad tiene y haya probablemente acumulado más toxina. Como principio, y por considerarlos portadores habituales de ciguatoxina, con frecuencia se prohíbe la venta de pescados carnívoros que habitan en arrecifes. El peligro se asocia con la acumulación de toxina en la cadena alimentaria, imposible de relacionar con ninguna floración de algas. El conteo de células en

el plancton no permite predecir si el pescado ha acumulado o no ciaguatoxinas. (Boutrif y Bessey, 2001).

9.2 Recomendaciones

Basado en las conclusiones anteriores, se hacen las recomendaciones siguientes:

1. Se necesitan datos sobre desarrollo de floraciones que tengan en cuenta las condiciones hidrográficas y climáticas y el estado nutricional de la columna de agua.
2. Deben hacerse estudios de toxicidad sobre los efectos luego de exposiciones repetidas a las toxinas marinas.
3. Deben continuar desarrollándose técnicas de química analítica capaces de separar, identificar y cuantificar toxinas marinas individuales.
4. Deben desarrollarse alternativas a los ensayos en ratón cuando ocurran eventos de floración no caracterizados. El énfasis en el uso de técnicas in vitro para floraciones caracterizadas debiera reducir el uso de ensayos en animales vivos.
5. Debe desarrollarse una base de datos, que incluya información básica de las biotoxinas marinas, sus estructuras químicas, sus propiedades físicas/químicas y métodos analíticos, que faciliten la aplicación rápida de métodos analíticos adecuados para las toxinas marinas.
6. Se requiere producir estándares y materiales de referencia certificados de toxinas puras, tanto para datos de toxicidad como para el desarrollo y la validación de técnicas analíticas.
7. Las organizaciones internacionales reconocidas-como el Comité Mixto FAO/OMS de Expertos en Aditivos Alimentarios (JECFA) y la Autoridad Europea de Inocuidad de los Alimentos deben ocuparse de las evaluaciones de riesgo formales basadas en datos toxicológicos y de exposición, científicos y sólidos. De carecerse de datos suficientes, puede encararse una consulta de expertos que explore las posibilidades de una adecuada evaluación de riesgos que sirva de base a reglamentos significativos.

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Este estudio ofrece una extensa revisión de diferentes aspectos relacionados con cinco síndromes de intoxicación por mariscos (intoxicación paralítica por mariscos, intoxicación diarreica por mariscos, intoxicación amnésica por mariscos, intoxicación neurológica por mariscos e intoxicación azapiracida por mariscos) y un síndrome de intoxicación por pescados. Se analizan en detalle diversos aspectos de los síndromes, las toxinas responsables producidas por organismos marinos, las estructuras químicas y los métodos de análisis, hábitat y presencia de los organismos productores de toxinas, estudios de caso y reglamentaciones vigentes. Se han realizado evaluaciones de riesgo basadas para cada toxina y elaborado recomendaciones para una mejor gestión de los riesgos, que permita reducir los efectos perjudiciales
de estas toxinas en la salud pública.